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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KOLKER, DANIEL E	
ART UNIT	**PAPER NUMBER**
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/828,548	SCHENK, DALE B.	
	Examiner	Art Unit	
	DANIEL KOLKER	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *177,196 and 198* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *177,196 and 198* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/11/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks and amendments filed 11 March 2008 have been entered. Claims 177, 196, and 198 are pending and under examination.

Maintained Rejections

Priority

2. The effective filing date for all pending claims is 7 April 1998 for the reasons previously made of record. Applicant did not traverse the examiner's determination that this is the appropriate effective filing date for the pending claims.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 177, 196, and 198 are rejected under 35 U.S.C. 103(a) as being unpatentable over Becker (EP 0 613 007, published 31 August 1994, of record) in view of Hanan (1996. Amyloid:Int J. Exp. Clin. Invest. 3:130-133, reference 182 on IDS filed 4 August 2005).

This rejection stands for the reasons of record. Briefly, Becker teaches administration of antibodies that bind to beta amyloid for treatment of Alzheimer's disease, which is on point to claims 177 and 196. Note that Becker specifically teaches that antibodies are to be administered to human patients; this limitation is newly added to claim 177 (see Becker, column 7 lines 49 – 52). The reference explicitly teaches therapeutic applications of the antibodies, specifically for treating Alzheimer's; see column 7 lines 32 – 52. The reference teaches that in vivo administration of antibodies is appropriate (column 7 lines 44 – 52). Becker explicitly teaches that Alzheimer's is due to aggregation of Aβ (column 1 lines 1 – 17), which is on point to claim 196, and teaches the intravenous route of administration is suitable for treatment of disease (column 8 lines 38 – 42), which is on point to claim 198. However Becker does not teach administration of antibody 10D5 as recited in claim 177.

Hanan teaches monoclonal antibody 10D5, which is on point to claim 177. The reference teaches that among the four monoclonal antibodies tested, 10D5 is the best in

inhibiting aggregation of Aβ peptide (p. 132, see also Figure 1). Hanan teaches that the results indicate that this discovery "may provide a factual basis for using monoclonal antibodies to prevent the β-amyloid formation that is associated with Alzheimer's disease" (p. 130, abstract). Hanan also teaches that the findings are on point to treatment of Alzheimer's disease, encompassed by claim 177 and recited in claim 196, by administering immunoglobulin molecules (p. 132, final paragraph). While Hanan teaches the efficacy of 10D5 antibody in disrupting Aβ aggregates and suggests it may be useful in developing treatments of Alzheimer's disease, the reference does not actually teach administration of the antibody to humans as recited in claim 177.

It would have been obvious to one of ordinary skill in the art to select the 10D5 antibody, taught by Hanan, to be administered for treatment of Alzheimer's disease as taught by Becker, with a reasonable expectation of success. The motivation to combine the teachings would be to select an effective antibody, as Hanan showed the superior efficacy of 10D5 in inhibiting Aβ aggregates, which both references recognized as playing an important role in development of the disease. Additionally, the reference by Becker specifically points to the intravenous route as an appropriate one, which is on point to claim 198

At p. 4 – 7 of the remarks filed 11 March 2008, applicant argues that the invention claimed would not have been obvious to one of ordinary skill in the art. Specifically, applicant argues:

1) Becker teaches combining Aβ with cells and determining whether an antibody can inhibit toxicity, whereas Hanan teaches an anti-aggregation assay. According to applicant, one of ordinary skill in the art would not have been able to tell how 10D5 disclosed by Hanan would behave in Becker's assay.

2) Hanan considered 10D5 as an antibody to be used in assay development, not for therapeutic treatment. That is, Hanan does not suggest treating Alzheimer's with this antibody.

3) The art did not provide a reasonable expectation of success, and the examiner has not given sufficient weight to statements of surprise at the success that were made by neutral experts upon learning of applicant's success.

4) The examiner has impermissibly used hindsight bias in setting forth and maintaining the rejection under § 103. In the absence of such hindsight, one of ordinary skill in the art would not have been motivated to do what applicant is now claiming.

Applicant's arguments have been fully considered but they are not persuasive. Each of the points listed above will be addressed in order.

With respect to 1), applicant argues that the artisan of ordinary skill would not know if Hanan's antibody would be suitable for treatment, because the artisan would not have known how the antibody would perform in Becker's assay. Becker does in fact teach certain assays, for example beginning at column 4 line 45. However in addition to such assays, Becker also explicitly teaches that antibodies raised against Aβ should be used to treat Alzheimer's. See for example column 7 lines 25 – 52. Even in the absence of performing any of the assays taught by Becker, the artisan of ordinary skill, upon reading the reference by Becker, would clearly understand that antibodies are to be administered to human patients in order to treat Alzheimer's disease. Becker specifically states that Alzheimer's is due to aggregation of Aβ (column 1 lines 1 – 17), so the artisan of ordinary skill would clearly be motivated, in determining which specific antibodies should be administered, to look for those which inhibit aggregation. As taught by Hanan, 10D5 is one such antibody and in fact it the most effective of several which were tested. Thus the artisan of ordinary skill would clearly have looked to 10D5 as a suitable antibody. See Hanan, p. 132 including Figure 1.

With respect to 2), applicant argues that "it does not appear that Hanan considered 10D5 as a candidate for therapeutic development" (remarks, p. 4, second paragraph). The examiner disagrees. The Discussion section of the reference by Hanan clearly speaks to using monoclonal antibodies to decrease aggregation of amyloidogenic proteins. See for example p. 132, second column, which states that "[t]he results of this study indicate that monoclonal antibodies raised against β-amyloid fragments prevented the formation of β-amyloid". While Hanan does not explicitly teach that this antibody is to be administered to human patients for treatment of Alzheimer's, the deficiency is cured by Becker, who teaches that antibodies to β-aymloid are to be administered for treatment of this disease. While Hanan speaks of "functional small antibody fragments" for treatment of disease, rather than intact antibodies as claimed, the reference by Becker indicates that either small fragments or intact antibodies can be used (Becker, column 5, final paragraph). Thus reading both references together, the artisan of ordinary skill would have been motivated to select 10D5 for administration to humans, as Hanan idicates the superior anti-aggregating effects of this particular antibody.

With respect to 3) applicant argues that the art did not provide a reasonable expectation of success, and argues that the examiner has not given sufficient weight to statements of

surprise at the success that were made by neutral experts. Applicant points to the article by Mandel which suggests that improper hindsight is frequently used in determination of obviousness. The examiner notes that several neutral experts did in fact express surprise at the success of applicant's work using either an antibody to β-amyloid or by administering β-amyloid protein, which then elicits antibodies. However, such statements of surprise do not negate the examiner's determination of obviousness. At the time the invention was made, there would have been a reasonable expectation of success. The reference by Becker clearly instructs an artisan of ordinary skill to administer anti-amyloid antibodies to patients with Alzheimer's in order to treat them. The reference by Majocha (U.S. 5,231,000, issued in 1993, previously cited) clearly states that antibodies against β-amyloid are to be used *in vivo* for diagnostic purposes (see for example column 5 lines 15 – 55 and claims 7 – 9). This reference, combined with the teachings of Becker, provide a reasonable expectation of success. Additionally Walker (1994. Journal of Neuropathology and Experimental Neurology 53:377-383, cited as reference 169 on IDS filed 4 August 2005) teaches that antibody 10D5 administered centrally to primates is able to label amyloid deposits in the brain (see p. 379 final paragraph and p. 382, last two paragraphs). This is on point to claims 177 and 196, note no particular route of administration is recited in these claims. Since 10D5 enters neurons and labels amyloid deposits, the reference by Walker indicates that the antibody is suitable for binding to β-amyloid following *in vivo* administration. Additionally, Walker provides a reasonable expectation of success in administration by other routes (i.e., intravenous, as recited in claim 198). Walker states that "[e]vidence that the blood brain barrier is deficient in Alzheimer's disease implies that some labeling from blood could occur without facilitated transport of ligands" (p. 382, end of first complete paragraph). Thus Walker clearly indicates that 10D5 antibody is suitable for administration and subsequent binding to amyloid-containing plaques within the brain. Walker even suggests that the antibody could be used for delivery of therapeutic agents. Although Walker did not recognize the potential of the antibody itself to be used as a therapeutic, the reference clearly demonstrates the *in vivo* efficacy of 10D5. Combined with the teachings of Becker and Hanan, this provides a reasonable expectation of success in treating Alzheimer's by administering 10D5 to a human.

With respect to 4), the examiner is aware of the possibility of hindsight bias and has worked diligently to avoid such bias. While the statements of neutral experts certainly have been considered, they have been weighed against the totality of the evidence of record and the

prior art references which teach every limitation of the claimed invention and do in fact provide the artisan of ordinary skill with a reasonable expectation of success.

For the reasons above, the rejection under 35 USC § 103(a) stands.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 177, 196, and 198 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 18 – 22 of copending Application No. 11/520438. Although the conflicting claims are not identical, they are not patentably distinct from each other because in the '438 case the claims require administration of humanized 10D5 rather than intact 10D5 as claimed here.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant did not traverse the examiner's determination of obviousness but indicated a terminal disclaimer may be provided in the future. No such disclaimer has been received, so the provisional rejection stands.

Conclusion

5. No claim is allowed.

6. The art made of record and not relied upon is considered pertinent to applicant's disclosure.

U.S. Patent Application 2006/0257396. The reference teaches and claims administration of 10D5 antibody for treatment of Alzheimer's disease. See for example claims 1, 5, and 23. However the reference does not qualify as prior art.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANIEL KOLKER whose telephone number is (571)272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel E. Kolker, Ph.D./
Patent Examiner, Art Unit 1649
May 30, 2008